NDA 19-758/SLR-041

MAR 17 2000

Novartis Pharmaceuticals Corporation
Attention: Mark Ammann
Director, Drug Regulatory Affairs
59 Route 10
East Hanover, NJ 07936

Dear Mr. Ammann:

Please refer to your supplemental new drug application dated September 29, 1999, received September 30, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Clozaril (clozapine).

This "Changes Being Effected in 30 days" supplemental new drug application provides for the addition of a **Geriatric Use** subsection under **PRECAUTIONS:**

> *Geriatric Use*
> *Clinical studies of clozapine did not include sufficient numbers of subjects aged 65 and over to determine whether they respond diferently from younger subjects.*
>
> *Orthostatic hypotension can occur with Clozaril (clozapine) treatment and tachycardia, which may be sustained, has been observed in about 25% of patients taking Clozaril (clozapine) (see WARNINGS, Adverse Cardiovascular and Respiratory Effects). Elderly patients, particularly those with compromised cardiovascular functioning, may be more susceptible to these effects.*
>
> *Also, elderly patients may be particularly susceptible to the anticholinergic effects of Clozaril (clozapine), such as urinary retention and constipation. (See PRECAUTIONS, Anticholinergic Toxicity)*
>
> *Dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. Other reported clinical experience does suggest that the prevalence of tardive dyskinesia appears to be highest among the elderly, especially elderly women (see WARNINGS, Tardive Dyskinesia).*

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert submitted September 29, 1999). Accordingly, the supplemental application is approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 3l4.80 and 314.81.

If you have any questions, call Steve Hardeman, R.Ph., Regulatory Management Officer, at (301) 594-2850.

Sincerely,

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research